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10/597,064	11/29/2007	Alicia Bertone	18525/04195	5421

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EXAMINER	
HARWARD, SOREN T	
ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/597,064	BERTONE ET AL.	
	Examiner	Art Unit	
	SOREN HARWARD	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *4-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 July 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20071024*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Search Notes*.

DETAILED ACTION

Election/Restrictions

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

When Claims Are Directed to Multiple Categories of Inventions:

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

1. Restriction is required under 35 U.S.C. 121 and 372. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1–3, drawn to a method of generating a nucleic acid database

II. Claims 4–12, drawn to an oligonucleotide array

III. Claims 13–19, drawn to a method of populating a nucleic acid database

IV. Claims 20–22, drawn to a method of observing changes in gene expression over time

V. Claim 23, drawn to a method of detecting infectious diseases

2. The inventions listed as groups I–V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack unity of invention because even though the inventions of these groups require the technical feature of analysis of mRNA sequences by microarrays or by computer databases, this technical feature is not a special technical feature as it was well known in the art before the date of invention.

3. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

4. The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention or species.

5. Should applicant traverse on the ground that the inventions have unity of invention (37 CFR 1.475(a)), applicant must provide reasons in support thereof. Applicant may submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. Where such evidence or admission is provided by applicant, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. During a telephone conversation with Milan Jovanovic on 6 July 2009 a provisional election was made without traverse to prosecute the invention of group I, claims 1–3. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4–23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

8. Applicant's claim under 35 U.S.C. 120 for the benefit of prior-filed Provisional Application Nr. 60/535111 is acknowledged.

Information Disclosure Statement

9. The information disclosure statement (IDS) submitted on 24 October 2007 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered in full by the examiner. A copy of the IDS signed by the examiner is being attached to this Office action.

Drawings

10. The drawings are objected to because the photographs in figure 5 are not of sufficient quality to permit adequate reproduction (see 37 CFR 1.84(b)). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

11. Claim 1 is objected to because “compete” in the third step appears to be a misspelling of "complete". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

12. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. In the third step of the method, sequences which are “3’-coding biased” are selected. This term is not defined with sufficient clarity within the disclosure. The claim suggests that “3’-coding biased” sequences are related to “5’-partial sequences having desirable characteristics”, but the disclosure does not describe the nature of these characteristics or the criteria by which they can be judged to be "desirable" or not. Hereinafter, this limitation will be interpreted as “sequences from the 3’ translated region of an mRNA”.

14. In the fourth steps of the method, sequences “derived from sequences that include poly-A tails” are claimed; the method or criteria of the derivation is not defined. Hereinafter, this limitation will be interpreted to mean “sequences from the 3’ UTR of an mRNA transcript”.

15. The flow of sequence selection between the steps is not clear. Step 5 "reduc[es] redundancy in selected sequences", but the group to which "selected sequences" refers is not clear; is it the coding sequences, the non-coding sequences, or a union of both? The input sequence set and output sequence set for step 6 is also imprecisely defined.

16. Finally, the last step of the method does not actually prepare a database, which appears to be the intended result of the method. If applicant intends to generate a database, then it is

suggested that the final step be stated as, "collecting all selected sequences into a nucleic-acid database".

Claim Rejections - 35 USC § 101

17. Claims 1–3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As established by the U.S. Supreme Court (see Benson, 409 U.S. 63; Diehr, 450 U.S. 175), and in accord with the decision in *In re Bilski* (545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008)), a claim to a process or method must meet one of two requirements to be eligible under 35 U.S.C. 101 as statutory subject matter. Either the critical steps of the method must be tied to a particular machine or apparatus, or the method must transform a particular physical article into another state or thing. In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter if and only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. 101 (i.e., a machine, manufacture, or composition of matter).

18. These claims are directed to a method of generating a database of nucleic acids. The method does not perform a real-world transformation of any physical article; it transforms only nucleic acid sequences (i.e., computational or mathematical abstractions). The claims also recite a series of calculations, but do not tie the method steps that are critical to the practice of the invention to any particular machine or apparatus. Even though carrying out such calculations by hand would be laborious and prone to error, the claim language does not preclude this possibility. The instant claims thus fail both parts of the eligibility test, and are therefore non-statutory.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai, *et al.* ("Functional annotation of a full-length mouse cDNA collection"), and further in view of Clamp, *et al.* ("Ensembl 2002: accommodating comparative genomics").

22. Claim 1 is directed to a method of preparing a species-specific nucleic acid database, comprising the following steps:

a. selecting species-specific coding and non-coding sequences from a general database

b. selecting sequences from the 3' translated or untranslated region of a transcript, which may include the poly-A tail

c. reducing redundancy in the selected sequences

d. comparing the non-redundant sequences to a set of annotated coding sequences, and filtering out sequences which do not meet a minimum level of

sequence homology; i.e., sequences for which an annotation cannot be reasonably inferred

e. creating a database of the remaining sequences

Kawai teaches a method of assembling and annotating a database of mouse cDNAs, which comprises the following steps:

a. aggregating results from mouse cDNA libraries (p. 685 § "Strategies")

b. selecting and grouping 3' end sequences from the library (p. 685 § "Strategies"), and possibly also including 3' UTR sequences (p. 687 § "Untranslated regions")

c. clustering and removing redundant sequences (p. 685 § "Strategies", § "Annotation of cDNAs")

d. comparing the non-redundant sequences to the MGI database to identify identical, similar, homologous, or related sequences (p. 685 § "Annotation of cDNAs", Fig. 2), and searching for mouse orthologues to human disease genes (p. 687 § "Orthologues of human disease genes")

e. creating a cDNA clone collection, which includes a database of all the sequences and their annotations (p. 688 § Discussion)

23. The method taught by Kawai differs from the method of this application in that Kawai aggregates sequences from mouse cDNA libraries, whereas the method of this application selects sequences from a non-species-specific sequence database. However, Kawai chose sequences from cDNA databases because the desired end result was a library of physical, tangible cDNA sequences to go along with the annotation database, and the easiest way to produce such a collection was to include only sequences for which physical cDNAs already existed. This application has no such restriction; a database will store a sequence just fine whether a corresponding physical copy exists or not.

24. The method taught by Kawai also differs from the method of this application in that Kaway does not filter out sequences that do not meet a minimum level of homology to sequences with a known annotation; or, stated differently, the minimum homology threshold used by Kawai is zero. However, Kawai clearly assigns sequences to categories that are ranked by their informativeness, from "MGI-confirmed" to "unclassifiable" (p. 686 Table 1). Removing uninformative data from a dataset is a well-known procedure in the art, and one skilled in the art at the time of invention would have removed less-informative sequences to lessen the amount of low-quality data. Said practitioner would be especially motivated to do triage based on sequence informativeness if the database could hold (or use) only a limited number of sequences, such as selecting only 3,200 sequences to be placed on a microarray.

25. Clamp teaches a method of automatically annotating sequences from a gene database (p. 48 §§ "Comparative genome analysis"), and provides examples of species-specific comparative annotation (p. 38 § "Introduction"). One of ordinary skill in the art at the time of invention would have recognized that the initial sequence-selection approaches of Kawai and Clamp are interchangeable with respect to generating a database; what is needed to practice the method is a set of transcribed protein sequences, and both an aggregated cDNA library or a query of a general database will provide the desired starting set of sequences. Said practitioner would have reasonably predicted that either sequence selection method would provide the necessary starting material for the method of database generation. Therefore, the invention is *prima facie* obvious.

26. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai and Clamp as applied to claim 1 above, and further in view of O'Brien, *et al.* ("The Promise of Comparative Genomics in Mammals").

27. Claim 2 is directed to generating a horse-specific nucleic acid database. Kawai teaches creation of a mouse-specific database, and does not teach creation of databases for other species. However, Clamp teaches generation of specific databases for humans and mice, and states that databases for *C. briggsae* (a nematode) and *A. gambiae* (a mosquito) are in progress (p. 38 § "Introduction"). O'Brien teaches comparative genomics in mammals, stating that genetic analysis techniques are broadly applicable across species (p. 458 § "Developing Mammalian Gene Maps"), and that genetic knowledge gained in one species can be extrapolated to others (e.g. p. 459 § "Biomedical Applications of Comparative Genomics with Rodent Models"). Genetic analysis of horses is specifically mentioned (p. 460 § "Mapping Agricultural Mammals"). Therefore, it is likely that at the time of invention, one of ordinary skill in the art would have regarded different species to be obvious variants of one another. And because the underlying genetic mechanisms of horses and mice are identical, one skilled in the art would have reasonably predicted that a method of generating a database of mouse genes would also perform successfully to generate a database of horse genes. The invention is therefore *prima facie* obvious.

28. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai and Clamp as applied to claim 1 above, and further in view of Frazer, *et al.* ("Cross-Species Sequence Comparisons: A Review of Methods and Available Resources").

29. Claim 3 is directed to using GenBank as the database from which the species-specific database is generated. Clamp teaches that the Ensembl sequences are aggregated from the sequencing projects themselves (p. 38 § "Introduction"), and Frazer teaches some complementary, interchangeable database sources for genetic information in the context of cross-species analysis (p. 2 §§ "Obtaining Genomic Sequences for Comparative Analysis", and p. 4 Table 1), and lists both NCBI (i.e., GenBank) and Ensembl as sources of general genetic

sequences. Just as one skilled in the art would have regarded an initial dataset of sequences from cDNA libraries and online databases to be obvious variants of one another, said practitioner is even more likely to have regarded initial datasets from different online databases to be obvious variants of one another. Thus, the invention is *prima facie* obvious.

Conclusion

30. No claim is allowed.

31. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Koonin, *et al.* ("Sequence similarity analysis of Escherichia coli proteins: Functional and evolutionary implications") teaches comparative analysis and functional identification of *E. coli* genes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SOREN HARWARD whose telephone number is (571)270-1324. The examiner can normally be reached on Mon-Thu 9:00-18:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JAMES O. WILSON can be reached on (571)272-0334. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Soren Harward/
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